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10/649,952	08/28/2003	Kenju Miura	58777.000013	7207

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,952	MIURA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 December 2005 and 23 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 07 December 2005 has been entered in full. Claims 16-25 and 28-34 are amended. Claims 35-37 are added. Claims 1-15 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 16-37 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 3-4 of the previous Office Action (07 June 2005) are *withdrawn* in view of the amended specification and title (07 December 2005).

2. The objection to claims 16-17, 21-25, and 32 at pg 4 of the previous Office Action (07 June 2005) is *withdrawn* in view of the amended claims (07 December 2005).

3. The rejection of claims 19-20 and 34 under 35 U.S.C. § 101 as set forth at pg 4 of the previous Office Action (07 June 2005) is *withdrawn* in view of the amended claims which now recite process steps (07 December 2005).

4. The rejections to claims 16-34 under 35 U.S.C. § 112, second paragraph, as set forth at pg 15-17 of the previous Office Action (07 June 2005) are *withdrawn in part* in view of the amended claims (07 December 2005). Please see section on 35 U.S.C. § 112, second paragraph below.

5. The supplemental information disclosure statement filed on 07 December 2005 has been considered.

Sequence Compliance

The Applicant's response to the notice to comply with Sequence Listing Requirements under 37 CFR §1.821 (07 December 2005) has been considered and is found persuasive. Therefore, the requirements set forth in the previous Office Action (07 June 2005) are withdrawn.

Information Disclosure Statement

6. Applicant provides a concise explanation of JP 08510998T2, Igaku, J. March 1994, Igaku, J. May 1994, and Moriyama et al. 1999. Applicant's explanations have been fully considered. However, Applicant must submit a new PTO/SB/08A form that lists the references so the Examiner can initial it.

Claim Rejections - 35 USC § 112

7. Claims 16-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: (1) a method of promoting the growth of hematopoietic stem cells and hematopoietic progenitor cells *in vitro* or *ex vivo* comprising administering human non-muscle type Cofilin of SEQ ID NO: 1 (and optionally, one or more cytokines) to hematopoietic stem cells or hematopoietic progenitor cells *in vitro* or *ex vivo* to promote growth and (2) a method of promoting the differentiation of hematopoietic stem cells and hematopoietic progenitor cells *in vitro* or *ex vivo* comprising administering human non-muscle type Cofilin of SEQ ID NO: 1 and one or more cytokines to hematopoietic stem cells or hematopoietic progenitor cells *in vitro* or *ex vivo* to promote differentiation, *does not* reasonably provide enablement for a method of treating a disease or for promoting growth or differentiation of hematopoietic stem cells, hematopoietic progenitor cells said method comprising administering at least one promoter of growth or differentiation of hematopoietic stem cells, hematopoietic progenitor cells, wherein said at least

one promoter includes Cofilin as an active ingredient. The specification also does not reasonably provide enablement for a method of regenerative medicine or expanding hematopoietic stem cells *ex vivo* by administering at least one promoter of growth or differentiation of hematopoietic stem cells, hematopoietic progenitor cells, or a combination thereof wherein said at least one promoter includes Cofilin as an active ingredient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth for claims 16-34 at pg 4-11 of the previous Office Action (07 June 2005).

The claims also recite that the Cofilin has the amino acid sequence depicted by SEQ ID NO: 1 or an amino acid sequence having at least 70% amino acid sequence homology with the amino acid sequence of Cofilin (SEQ ID NO: 1) or the amino acid sequence of Cofilin except that it has 1-5 amino acid deletions, substitutions, additions, or combinations thereof, said Cofilin having the activity of promoting growth and differentiation of hematopoietic stem cells, hematopoietic progenitors, or a combination thereof. The claims recite that the Cofilin is encoded by the base sequence depicted by SEQ ID NO: 2 or DNA comprising a base sequence having at least 70% base sequence homology with the base sequence of Cofilin depicted by SEQ ID NO: 2, said Cofilin having the activity of promoting growth and differentiation of hematopoietic stem cells, hematopoietic progenitors, or a combination thereof. The claims recite that the disease comprises panhematopenia, a disease accompanied by hematopoietic hypofunction.

Applicant's arguments (07 December 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the claimed invention is drawn to methods that require the administration of at least one promoter that has the activity of Cofilin of promoting growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors. Applicant argues that the claimed methods are limited to administering only those Cofilin proteins that have the activity of promoting growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors. Applicant contends that one of skill in the art may determine whether a particular Cofilin protein has the activity of promoting growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors using routine experimentation disclosed in the specification.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action of 07 June 2005, the instant specification discloses that "when the term "Cofilin" is used without any qualification in the present invention, it covers not only Cofilin having the amino acid sequence depicted by SEQ ID NO: 1 but also its analogous compounds" (pg 11, lines 2-4). The specification then teaches the numerous analogous compounds that are encompassed by the invention (pg 11, [44]; see also pg 8 of previous Office Action). However, the specification does not teach any variant, fragment, or derivative of the human non-muscle type Cofilin protein other than the full-length amino acid sequence of SEQ ID NO: 1. The specification also does not teach functional and structural characteristics of the polypeptide variants, fragments, and derivatives recited in the claims. The broad brush discussion of making and screening for Cofilin variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the Cofilin polypeptide of SEQ ID NO: 1 is disclosed. Based upon the relevant literature's

disclosure of numerous Cofilin proteins and Cofilins' known activities (such as actin filament turnover) and cell expression patterns (see for example, Vartiainen et al. Molec Biol Cell 13: 183-194, 2002; pg 183-184, 192; Maciver et al. Genome Biol 3(5): 1-12, 2002, especially pg 7, 2nd and 3rd full paragraphs in col 2), one skilled in the art would not predict that any Cofilin, except full-length human non-muscle type Cofilin (as disclosed in the examples of the instant specification), would promote the growth or differentiation of hematopoietic stem cells and hematopoietic progenitor cells. Furthermore, according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis". The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such trial and error experimentation is considered undue. Certain positions in the polypeptide sequence are critical to the protein's structure/function relationship, e.g., such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al.,

1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Additionally, although claims 22 and 24 have been amended to include hybridization conditions, the conditions encompass a broad range of hybridization temperatures (for example, 45-68°C and 25-50°C), which may not remove the polynucleotide variants associated with non-specific hybridization. For example, the state of the art teaches that in the hybridization reaction, "choices of buffer, temperature, and time are never trivial because these effectors in combination with membrane, probe, label, and target form a complex network of cause and effect" (Herzer and Englert. "Nucleic Acid Hybridization". (2001) Molecular Biology Problem Solver: A Laboratory Guide. New York:Wiley-Liss, page 424). Herzer and Englert also state that "[a] hybridization temperature that is too low will manifest itself as a high nonspecific background...and thus hybridization temperature can't be exactly predicted" (pg 425, 3rd full paragraph; see also Figure 14.8 at page 452). Therefore, the claims do not recite meaningful structural limitations and one of skill in the art would not be apprised of the metes and bounds of the hybridization conditions or the varying structures of the polynucleotides produced.

Thus, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the Cofilin protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity.

As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). It is also noted that according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of the claim, then this great quantity of experimentation should be considered in the overall analysis".

(ii) Applicant submits that in the "Background of the Invention" of the specification, previous methods of treating diseases that result from insufficient growth or differentiation of hematopoietic stem or progenitor cells are described. Applicant points out that previous methods showed that agents that promote the growth and/or differentiation of hematopoietic stem or progenitor cells are useful in treating diseases associated with hematopoietic hypofunction caused by anti-cancer agents, radiation, etc. Applicant asserts that the specification shown Cofilin promotes the growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors. Applicant argues that one of ordinary skill in the art armed with the instant specification would readily appreciate that Cofilin may be used in treating diseases that result from insufficient growth or differentiation of hematopoietic stem or progenitor cells.

Applicant contends that those of ordinary skill in the art can easily determine the route of administration, as well as the appropriate dose and/or dosing period. Applicant states that an undue quantity of experimentation would not be required by one skilled in the art to carry out the invention.

Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner acknowledges that the state of the art is such that various other cytokines and hematopoietic growth factors have been utilized to treat a number of diseases and conditions associated with hematopoietic hypofunction. However, neither the prior art nor the specification of the instant application teach the administration of any Cofilin protein to any subject for the promotion of growth and differentiation of hematopoietic stem cells or progenitor cells. The specification also does not teach the treatment any diseases that result from insufficient growth or differentiation of hematopoietic stem cells or hematopoietic progenitors comprising the administration of any Cofilin. The prophetic examples of administration techniques and dosages of Cofilin set forth at pg 16, paragraphs [57-58] of the specification are not adequate guidance, but are merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The present invention is also unpredictable and complex wherein one skilled in the art may not necessarily treat all diseases that result from insufficient growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors by administration of Cofilin. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease and to determine the route of administration of the Cofilin, as well as quantity and duration of treatment. One skilled in the art would not be able to predict that administration of a Cofilin protein would treat any disease or promote the growth and

differentiation of hematopoietic stem and progenitor cells *in vivo*. For example, the state of the art is such that the goal of delivering proteins and peptides noninvasively has only achieved modest success, with poor applicability to proteins and peptides (pg 343, col 1-2; Pettit et al. Trends Biotechnol 16: 343-349, 1998). The problems posed by proteins and peptides is their large molecular size, electrical charge, relatively hydrophilic nature, and relative instability in environments of extreme pH or proteolytic activity (such as the stomach and intestine) (pg 343, col 2). Pettit et al. review several routes of protein administration and the limitations that have been encountered. For example, limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (pg 344-345). Much effort has been given to the transdermal delivery of pharmaceutical products, but clinical applications have been limited to non-protein drugs because of the skin's poor permeability to proteins and peptides (pg 343, col 2). Additionally, proteins or peptides administered systemically must resist clearance via molecular filtration by the kidney and clearance by the reticuloendothelial system (pg 345, col 2). Although the pulmonary delivery route has generated the most encouraging data, the bioavailability of proteins (i.e. the amount of protein that crosses from the alveoli in to the pulmonary circulation) is dependent on the physical characteristics of the delivered protein and is not the same for proteins and peptides in general (pg 343-344). Therefore, the state of the prior art establishes the unpredictability of delivering proteins to a subject.

(iii) Applicant argues that the specification teaches that the administration of human non-muscle type Cofilin alone promotes the expansion of HPP-CFC (Figure 4, paragraphs [107-108]). Applicant indicates that by demonstrating that the administration of human non-muscle type Cofilin alone induces HPP-CFC to proliferate, human non-muscle type Cofilin alone is able to promote the differentiation of hematopoietic stem cells or hematopoietic progenitor cells.

Applicant's arguments have been fully considered but are not found to be persuasive. As indicated in the previous Office Action, the specification of the instant application discloses that human non-muscle type Cofilin of SEQ ID NO: 1 promotes the growth (proliferation) of hematopoietic stem cells and hematopoietic progenitor cells *in vitro/ex vivo* (pg 33, [107-108]; Figures 4, 5). However, the specification does not teach that human non-muscle type Cofilin *alone* is able to promote the differentiation of hematopoietic stem cells or hematopoietic progenitor cells. The instant specification (pages 36-39) and Figures 6B-6D, 7, 8, and 9 clearly indicate human nonmuscle-type Cofilin only in combination with SCF and FL or TPO causes differentiation of hematopoietic stem and progenitor cells. The specification and the prior art teach that "differentiation" means both the change of hematopoietic stem cells into hematopoietic progenitors and the change of hematopoietic progenitors into mature cells (see for example, pg 10 paragraph [41]; Szilvassy, S Arch Med Res 34: 446-460, 2003; Figure 1). Hematopoietic progenitor cells include, for example, CFU-GM, BFU-E, CFU-Mk, CFU-Mix (specification pg 10, paragraph [40]; Szilvassy, Figure 1). In the instant application's experimental results shown in Figure 6B (measuring colony formation of CFU-GM), Figure 6C (measuring colony formation of BFU-E), and Figure 6C (measuring colony formation of CFU-Mix) as compared to controls, the Cofilin alone group is similar to the PBS and Input controls.

Thus, Cofilin in combination with SCF and FL or TPO is required for hematopoietic stem and progenitor cell differentiation. Szilvassy also teaches that proliferation and differentiation are not necessarily strictly coupled (pg 446, bottom of col 2). Furthermore, regarding the activity of recombinant human nonmuscle-type Cofilin in human megakaryocyte proplatelet formation, the specification states that "no proplatelet formation was visible when the human nonmuscle-type Cofilin or TPO was added singly" (pg 39, paragraph [127]). Therefore, one skilled in the art would not be able to predict that Cofilin alone would promote the differentiation of hematopoietic stem cells or hematopoietic progenitor cells *in vivo*, *in vitro*, or *ex vivo*.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to treat all possible diseases that result from insufficient growth and differentiation of hematopoietic stem/progenitor cells comprising administering any Cofilin protein, to determine the optimal quantity, duration, and type of administration of Cofilin, and to generate the infinite number of derivatives recited in the claims and possibly screen same for activity; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural and functional limitations and Cofilin protein limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

8. Claims 16-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 16-34 at pg 12-15 of the previous Office Action (07 June 2005).

The claims are directed to a method of promoting growth or differentiation of hematopoietic stem cells, hematopoietic progenitor cells or a combination thereof or a method of treating a disease that results from insufficient growth or differentiation of hematopoietic stem and/or progenitor cells comprising administering at least one promoter of growth or differentiation, wherein said at least one promoter includes Cofilin. The claims are also recite a method of promoting the growth or differentiation of hematopoietic stem cells, hematopoietic progenitor cells, or combinations thereof, comprising administering human non-muscle type Cofilin to hematopoietic stem cells, hematopoietic progenitor cells, or combinations thereof.

(i) Applicant states that the claimed methods are limited to administering only those Cofilin proteins that have the activity of promoting growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors. Applicant asserts that the present application claims a novel and unobvious method employing a known set of proteins. Applicant indicates that Cofilin proteins are known in the art to constitute a family of actin-binding proteins. Applicant states that Cofilin in every higher vertebrate animal each consist of 166 amino acids. Applicant cites *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005) and emphasize that they should no be required to describe that which is already known. Applicant argues that the activity of Cofilin in

promoting the growth and/or differentiation of hematopoietic stem and/or hematopoietic progenitors may be determined with reference to the activity in promoting the expansion of HPP-CFCs.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the specification of the instant application teaches that "when the term 'Cofilin'' is used without any qualification in the present invention, it covers not only Cofilin having the amino acid sequence depicted by SEQ ID NO:1 but also its analogous compounds" (pg 11, lines 2-4). The specification continues to disclose that "analogous compounds of Cofilin as referred to in the specification include the following which all have the activity of promoting the growth and/or differentiation of hematopoietic stem cells and/or hematopoietic progenitors: one comprising the amino acid sequence of Cofilin depicted by SEQ ID NO:1 except that it has one or more amino acid deletions, substitutions and/or additions; one comprising an amino acid sequence encoded by a base sequence hybridizable under stringent conditions with a base sequence complementary to the base sequence coding for the amino acid sequence of Cofilin depicted by SEQ ID NO:1; and one comprising an amino acid sequence having at least 30%, preferably at least 50%, more preferably at least 60%, and most preferably at least 70%, amino acid sequence homology with the amino acid sequence of Cofilin (SEQ ID NO:1)" (pg 11, [44]).

However, the description of one Cofilin polypeptide species (SEQ ID NO: 1), is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all variants, fragments, and derivatives or an entire genus of methods of using those variants, fragments, and derivatives. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing

identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. However, in the instant case, there is no identification of any particular portion of the structure that must be conserved in order to conserve the required function or that the described function is truly representative of all members of the claimed genus. Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus of methods that utilize the genus of Cofilin proteins. The skilled artisan cannot envision the Cofilin proteins of the encompassed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. The broad brush discussion of making and screening for variants in the instant specification does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the Cofilin polypeptide of SEQ ID NO: 1 is disclosed.

It is noted that the fact pattern of the case cited by the Applicant and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections. For instance, in *Capon v. Eshhar*, the nucleotide sequences utilized to generate a chimeric gene were structurally and functionally characterized in the prior art. The novelty of the invention was the combination of the segments to achieve a novel chimeric gene. However, in the instant application, there are no teachings in the prior art or the specification that identify portions of any Cofilin protein (human or nonhuman; non-muscle type or muscle type) that must be conserved in order to conserve the required function. Applicant has not described

or shown possession of the genus of methods of using an entire genus of functionally equivalent Cofilin polypeptides which incorporate all variants, fragments, and derivatives. Therefore, only methods of utilizing the human non-muscle type Cofilin of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 112, second paragraph

9. Claims 20 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The basis for this rejection is set forth for claims 20 and 34 at pg 16-17 of the previous Office Action (07 June 2005).

10. The term "regenerative medicine" in claims 20 and 34 is a relative term which renders the claims indefinite. The term "regenerative medicine" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined what method steps, products, and/or endpoints are encompassed by this phrase.

Applicant asserts that the term "regenerative medicine" is a term that is known and used in the art. Applicant states that a search for the term resulted in the term being present in 192 U.S. published patent applications. Applicant indicates that one of skill in the art would be reasonably apprised of the scope of the invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Simply indicating that the term "regenerative medicine" is present in 192 U.S. published patent applications still does not define what method steps, products, and/or endpoints are encompassed

by this phrase in this application. Each patent application is examined on its own merits and thus, the other applications may have defined different meanings for the term "regenerative medicine". One of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, does the term encompass organ regeneration? Brain regeneration? Skin regeneration? Limb regeneration?

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
28 February 2006

ELIZABETH KEMMERER
PRIMARY EXAMINER